III. Remarks

A. Status of Claims

Claims 75-77, 82, 85, 89, and 91 have been amended without prejudice or admission.

Claim 75 has been amended to recite "hydrophobic means for sequestering the opioid antagonist," incorporate features of claim 89 and 91, and to recite that "an amount of the opioid antagonist released from the dosage form which has been subjected to tampering is an amount bioequivalent to 0.25 mg of naltrexone or more ...." It is respectfully submitted that support for these amendments can be found, e.g., on page 7, lines 7-38, page 10, lines 5-14, page 66, lines 15-19, page 28, line 25, to page 31, line 30, of the original specification. Specific support for "a dissolution bath" can be found, e.g., on page 68, lines 10-12, of the original specification.

Claims 76 and 77 has been amended to recite "hydrophobic means for sequestering" and to correct a typographical error. It is submitted that support for these amendments can be found, e.g., on page 28, line 25, to page 31, line 30, of the original specification.

Claim 82 has been amended to depend from claim 80, instead of claim 75.

Claim 85 has been amended to remove the term objected to by the Examiner, and to recite that "the physiological effect is prevention or reversal of the effects of opioids." It is respectfully submitted that support for this amendment can be found, e.g., on page 24, line 19, of the original specification.

Claim 89 has been amended to recite that "the amount of the antagonist released at 1, 2, 4 and 12 hours from the intact dosage form ... is undetectable by High Performance Liquid Chromatography." It is submitted that support for this amendment can be found, e.g., on page 68, lines 5-10, of the original specification.

Claim 91 has been amended to recite that "the amount of the antagonist released from the dosage form which has been orally administered intact is bioequivalent to 0.025 mg of naltrexone or more." It is respectfully submitted that support for this amendment can be found, e.g., on page 8, line 20, of the original specification.

New claim 92 has been added. It is submitted that support for new claim 92 can be found, e.g., on page 29, line 36, to page 30, line 31.

Claims 75-86, 89, 91 and 92 are pending.

It is respectfully submitted that the elected invention is encompassed by claims 75-86, 89, 91 and 92.

B. Claim Rejections – 35 U.S.C. § 112

Claims 75 and 85 have been rejected under 35 U.S.C. 112, first paragraph, allegedly as failing to comply with the enablement requirement. The Examiner stated that "[i]t is unclear to the Examiner as to how the instant invention can 'prevent' such euphorigenic effects using the composition claimed herein." *See, Office Action, page 4.* The Examiner suggested that the limitation "prevention of euphorigenic effects of opioids" in claim 85 be removed to overcome this rejection. *See, Office Action, page 5.*

The rejection is respectfully traversed.

The objected term has however been removed from claim 85, in an effort to advance prosecution.

Withdrawal of the rejection is respectfully requested.

C. Claim Rejections – 35 U.S.C. § 112

Claim 82 has been rejected under 35 U.S.C. § 112, second paragraph, for having insufficient antecedent basis for "the opioid agonist" in line 2.

Claim 82 has been amended without prejudice to depend from claim 80, instead of claim 75. It is respectfully submitted that claim 80 provides sufficient antecedent basis for "the opioid agonist."

Withdrawal of the rejection is respectfully requested.

D. Claim Rejections – 35 U.S.C. § 103

1. U.S. Patent No. 4,987,136 to Kreek et al.

Claims 75-79, 83-86, 89 and 91 have been rejected under 35 U.S.C. § 103(a) over U.S. Patent No. 4,987,136 to Kreek et al. ("the Kreek reference").

The rejection is respectfully traversed.

Independent claim 75 recites in part that "an amount of the opioid antagonist released from the dosage form which has been orally administered intact ... is **insufficient** to produce a physiological effect of the opioid antagonist in a human patient."

The Kreek reference in contrast states that the opioid antagonists "are used to **treat** clinical gastroenterorologic disorders ...." *See column 2, lines 30-32.* The Kreek reference simply does not provide a reason for a skilled person to formulate a dosage form such that "an amount of the opioid antagonist released from the dosage form which has been orally administered intact is **insufficient** to produce a physiological effect of the opioid antagonist."

In an effort to advance prosecution and further differentiate from the cited reference, claim 75 has been amended to recite that "the intact dosage form releases less than 15% by

weight of the opioid antagonist within 36 hours, based on the in-vitro dissolution in a dissolution bath," and that the amount of the opioid antagonist released "from the dosage form which has been administered intact is less than an amount bioequivalent to 0.125 mg of naltrexone." It is respectfully submitted that these amendments further distinguish the dosage form of claim 75 from the Kreek reference.

In response to the Examiner's statement on page 6 of the Office Action that "the dosage form 'not posing a risk of precipitation of withdrawal' and 'the opioid antagonist not being bioavailable when the dosage form is intact' (claims 83 & 84 respectively)," Applicants submit that these features are appropriate functional limitations; and respectfully request that the features be considered in determining patentability of the claims. *MPEP, section 2173.05(g); In re Schreiber, 128 F3d 1473 (CAFC 1997); Rowe v. Dror, 112 F33d 473 (CAFC 1997); Pitney Bowes, Inc. v. Hewlett-Packard Co., 182 F3d 1298 (CAFC 1999).*

In response to the Examiner's statement on page 6 of the Office Action with regard to the claimed ratios being "variable parameters that can be attained using routine experimentation," Applicants submit that the desirability of the specific ratio recited in claim 79 is not suggested by the Kreek reference because the Kreek reference does not describe this ratio. Applicants respectfully note that "obviousness cannot be proven merely by showing that a known composition could have been modified by routine experimentation or solely on the expectation of success; it must be shown that those of ordinary skill in the art would have had some apparent reason to modify the known composition in a way that result in the claimed composition." *In Ex Parte Whallen II, Appeal No. 2007-4423, Decision of Appeal dated July 23, 2008.* The Kreek reference does not provide such a reason in the present case.

For the foregoing reasons, withdrawal of the rejection is respectfully requested.

2. <u>U.S. Patent No. 6,277,384 to Kaiko et al.</u>

Claims 75-86, 89 and 91 have been rejected under 35 U.S.C. § 103(a) over U.S. Patent No. 6,277,384 to Kaiko et al. ("the Kaiko reference").

The rejection is respectfully traversed, for the reasons set forth in the response filed on September 3, 2008.

In an effort to advance prosecution and further differentiate over the cited reference, claim 75 has been amended to recited that the hydrophobic means for sequestering the opioid antagonist is such that "the intact dosage form releases less than 15% by weight of the opioid antagonist within 36 hours, based on the in-vitro dissolution in a dissolution bath," and that "an amount of the opioid antagonist released from the dosage form which has been orally administered intact is less than an amount bioequivalent to 0.125 mg of naltrexone." Claim 75 also recites that the amount of the opioid antagonist released from the dosage form which has been administered intact "is insufficient to produce a physiological effect of the opioid antagonist in a human patient."

The Kaiko reference describes dosage forms which are "aversive in a physically dependent subject" and provide "at least a mildly negative, 'aversive' experience in physically dependent addicts". *See, e.g., Abstract.* The Kaiko reference does not therefore suggest an oral dosage form wherein "the hydrophobic material sequesters the antagonist" and which releases "less than 15% by weight of the opioid antagonist within 36 hours, based on the in-vitro dissolution in a dissolution bath," "less than an amount bioequivalent to 0.125 mg of naltrexone" and the amount which "is insufficient to produce an antagonist effect of the antagonist" as recited in claim 75.

In response to the Examiner's statement on page 9 of the Office Action that "suitable or effective amounts can be determined by one of ordinary skill in the art through routine or manipulative experimentation to obtain optimal results," and on page 11 of the Office Action "that the determination of effective or suitable ratios is within the level of one of ordinary skill in the art through routine experimentation to obtain optimal results," Applicants respectfully note that "obviousness cannot be proven merely by showing that a known composition could have been modified by routine experimentation or solely on the expectation of success; it must be shown that those of ordinary skill in the art would have had some apparent reason to modify

the known composition in a way that result in the claimed composition." *In Ex Parte Whallen II, Appeal No. 2007-4423, Decision of Appeal dated July 23, 2008.*

Withdrawal of the rejection is respectfully requested.

3. WO 97/33566 to Kuczynski et al.

Claims 75-86, 89 and 91 have been rejected under 35 U.S.C. § 103(a) over WO 97/33566 to Kuczynski et al. ("the Kuczynski reference").

The rejection is respectfully traversed.

In an effort to advance prosecution, claim 75 has been amended to recite "**hydrophobic** means for sequestering the opioid antagonist."

There is simply no description in the Kuczynski reference of the "**hydrophobic** means for sequestering the opioid antagonist" recited in claim 75.

In response to the Examiner's reliance on "[a]dditional cellulose polymers ... disclosed in Example 5, on pages 8-9 and include[ing] carboxymethylcellulose" of the Kyczynski reference, Applicants respectfully note that the disclosure of "carboxymethylcellulose" on page 8, line 28, in the Kuczynski reference is with regard to an opioid **agonist** composition, rather than an antagonist composition.

With further regard to new claim 92, it is respectfully submitted that the Kuczynski reference does not teach or suggest a dosage form where the sequestering means comprises "an acrylic polymer" as recited in claim 92.

Withdrawal of the rejection is therefore respectfully requested.

IV. Conclusion

An early and favorable action on the merits is earnestly solicited. According to currently recommended Patent Office policy, the Examiner is requested to contact the undersigned by telephone in the event that a telephonic interview will advance the prosecution of this application.

Respectfully submitted,
DAVIDSON, DAVIDSON & KAPPEL, LLC

By: _____
Oleg Ioselevich
Reg No. 56,963

Davidson, Davidson & Kappel, LLC
485 Seventh Avenue, 14th Floor
New York, New York 10018
(212) 736-1940